

of allergy/atopy), the child's diet should exclude cow's milk for the first year of life, eggs for two years, and peanuts for three years. Risk and severity may also be reduced by environmental controls to avoid exposure to dust mites and tobacco smoke.

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Immunization Update

THE 1997 RECOMMENDED IMMUNIZATION Schedule for Children reflects several important changes, including the recommended use of acellular pertussis vaccines combined with tetanus and diphtheria toxoids (DTaP) for use in infants; increased use of inactivated poliovirus vaccine (IPV) for healthy children; and guidelines for delivery of immunizations to adolescents. In addition, approval is expected for several new vaccines.

Pertussis

Three DTaP products have been approved for the primary series in infancy: ACEL-IMUNE, Infanrix, and Tripedia. In European clinical trials, these products were 80-89% efficacious for preventing pertussis, comparable to or better than the efficacy of whole-cell pertussis vaccines used in the United States. DTaP also causes fewer reactions (fever, irritability, swelling) than whole-cell preparations and is therefore preferred. Whole-cell vaccine is an acceptable alternative, however. It has the advantage of being combined with *Haemophilus influenzae* type b (Hib) vaccines for use in infancy, thus decreasing the number of injections administered. Tripedia combined with Hib (TriHIBit) is approved for children 15 months of age and older. The manufacturer anticipates FDA approval for use in infants in the summer of 1997.

Hepatitis B

All infants should be immunized against hepatitis B (Hep B), and all adolescents not previously immunized should be vaccinated. There are two hepatitis B products, Energix B and Recombivax, which can be used interchangeably if necessary. Energix B has received approval for the same dose (10 µg) to be used for all children from birth through 19 years of age. Recombivax is approved as a 2.5-µg dose through 10 years of age for children born to HBsAg-negative women, and as a 5-µg dose from 11 to 19 years of age for children born to HBsAg-negative women and for children of all ages born to HBsAg-positive

women. COMVAX, a new combination product containing Hib (PRP-OMP) and Recombivax (5 µg), has recently become available. COMVAX can be used for routine immunization of all children 6 weeks of age and older.

Hepatitis A

Two hepatitis A vaccines (Havrix and VAQTA) have been licensed for children 2 years of age and older. The vaccines are indicated for children with chronic liver disease and those traveling to areas with high rates of hepatitis A or living in high-risk communities.

Polio

Thanks to the intense efforts coordinated by the Pan American Health Organization, the Western Hemisphere has been free of paralytic polio caused by wild-type poliovirus since 1991. The target for global eradication is the year 2000. Because of the decreased risk of exposure to wild-type polioviruses and the 8 to 10 cases per year of vaccine-associated paralytic polio, the US routine immunization schedule now emphasizes the increased use of IPV. Advisory groups consider the use of IPV alone, OPV alone, or a sequential schedule of two doses of IPV followed by two doses of OPV to be acceptable immunization schedules. The Advisory Committee on Immunization Practices (ACIP) gives preference to the sequential schedule, as this will prevent 50-75% of the 8 to 10 cases of vaccine-associated paralytic polio while maintaining optimal intestinal immunity in the general population.

Varicella

The recently released ACIP recommendations on varicella vaccine are consistent with the 1995 American Academy of Pediatrics guidelines. Both call for universal immunization of healthy children 1 year of age or older who have not had chicken pox. The varicella vaccine (Varivax) is also strongly recommended for all susceptible people in contact with immunocompromised children. The risk of the vaccine virus being transmitted from a vaccinated child to a close contact is minimal and is far outweighed by the benefits of immunization. One dose of Varivax is recommended for children under 13 years of age, two doses at 13 years and older.

Combination Products

The number of injections required to immunize children fully has increased, but combination products will help correct this problem. Two new combination products have been approved recently. COMVAX is available for use in infants and children, and TriHIBit is approved for use at 15 months or older. Currently TriHIBit must be mixed by the health care professional before administration, but should be available as a single product by mid-1997. Other combination products including DTaP/Hep B, DTaP/IPV/Hib, and DTaP/IPV/Hep B are being developed, and several manufacturers hope to produce a DTaP/Hep B/Hib/IPV combination for use at 2, 4, and 6 months of age. Thus, practitioners will shortly have several combination products from which to choose.

Because not all components of combined vaccines are identical, problems may arise if some children receive one or more extra doses of some antigens when practitioners change products or when children change doctors.

The Future

Rotavirus vaccine may be licensed within the next year. Conjugated pneumococcal vaccines may be available in the next few years. Respiratory syncytial virus and cytomegalovirus vaccines are still in research development.

Immunizations are among the most cost-effective means available for improving health. The improvement in children's health as a result of new vaccines added to the immunization schedule is most clearly illustrated by the Hib conjugate vaccines. Since widespread use beginning a decade ago, invasive Hib disease has virtually disappeared. New vaccines promise to eliminate other harmful infectious diseases.

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The Use of Umbilical Cord Blood Stem Cells for Hematopoietic Reconstitution

HEMATOPOIETIC PROGENITOR CELLS, or stem cells, are pluripotent precursors to the entire blood and immune systems. Umbilical cord blood from newborns is the newest source of stem cells used to reconstitute a deficient hematopoietic system. The use of umbilical cord blood stem cells has been successful in more than 300 children and holds great promise as a principal source of stem cells.

Bone marrow transplantation (BMT) is still effective therapy for children with aplastic anemia, certain malignancies, and some genetic disorders. Historically, most transplants have been performed with marrow from human leukocyte antigen (HLA)-matched siblings. Engraftment with transplanted bone marrow takes about 2 weeks for neutrophils and 3–4 weeks for platelets. Donating cells for BMT is painful, may induce anemia, and incurs the risks of general anesthesia.

Since most potential recipients do not have related histocompatible donors, peripheral blood and umbilical cord blood provide alternative sources of hematopoietic stem cells. Stem cells from peripheral blood are obtained from the patient or a histocompatible donor. Cytokines, such as granulocyte colony-stimulating factor (G-CSF),

are used to mobilize stem cells from the bone marrow to the peripheral blood. If the patient's own blood is used, chemotherapy usually occurs first. Engraftment with peripheral blood stem cells takes about a week less than with BMT.

The presence of significant numbers of stem cells in placental blood suggests the potential utility of umbilical cord blood as a source of stem cells for transplantation. At the time of delivery, the blood from the umbilical cord (usually 75–150 cc) can be collected and stored to give to the patient at a later time.

Umbilical cord blood has many advantages. Collection carries no risk to the donor. Ethnic diversity of HLA types is easy to achieve through a stem cell banking system. Contamination with viruses is uncommon. Search time for a compatible donor is minimized because HLA typing is done at the time of collection. Frozen stem cells have a very long—possibly indefinite—shelf life. Shipment and thawing are simple, so stem cells are available virtually on demand, minimizing delay to transplantation. There is also some evidence from preliminary clinical trials that, even when the donor and recipient are not histocompatible, the risk of graft-versus-host-disease (GVHD) after umbilical cord blood transplantation is reduced compared with bone marrow transplantation from unrelated HLA-matched donors.

Umbilical cord stem cells do carry potential disadvantages. Because of the small volume of cord blood, there is no back-up in the event of graft failure, and there may not be sufficient quantities of stem cells to reconstitute an adult recipient. Maternal consent is required for testing of placental blood for infectious agents, genetic disorders, and drugs. Engraftment using cord blood averages 24 days for neutrophils and 72 days for platelets. Theoretically, the risk of tumor recurrence may increase because of a decreased risk of GVHD compared to BMT. There is a potential risk of contamination of umbilical cord blood specimens, either by bacteria or by maternal T lymphocytes that cross from the mother to the infant before delivery, although this has not yet been a clinical problem. Finally, storage of umbilical cord blood is costly—\$1,000 to 1,500—and requires special quality controls.

Studies are in progress to establish standards for collection of umbilical cord stem cells and to determine the safety and utility of this source of stem cells in hematopoietic reconstitution. Stem cell expansion *in vitro* may increase the ability of cord blood to reconstitute hematopoiesis in larger recipients. Furthermore, umbilical cord blood stem cells may become an ideal target for gene therapy for patients with genetic disorders. Significant ethical issues remain to be resolved regarding the collection and utilization of placental stem cells.

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